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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/550,760	09/27/2005	Anders Ljunggren	133087.09001	3784

52286 7590 12/14/2009

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EXAMINER	
THOMAS, TIMOTHY P	
ART UNIT	PAPER NUMBER
1628	

MAIL DATE	DELIVERY MODE
12/14/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/550,760	LJUNGGREN ET AL.	
	Examiner	Art Unit	
	TIMOTHY P. THOMAS	1628	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 October 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11 and 14-25* is/are pending in the application.

4a) Of the above claim(s) *14-16 and 21-25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11 and 17-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/5/2009 has been entered.

Response to Arguments

2. Applicants' arguments, filed 10/5/2009, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

3. Applicant's arguments with respect to claims 11 and 17-20 have been considered but are moot in view of the new ground(s) of rejection.

Claim Rejections - 35 USC § 103

4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

5. Claims 11 and 17-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Imura et al. (US 2003/0187038; 2003; filed 2001; cited in a prior Office Action); and Yoneyama, et al. ("Cardiovascular Effects of L-158,809, a New Angiotensin Type 1

Receptor Antagonist, Assessed Using the Halothane-Anesthetized In Vivo Canine Model"; 2002; Jpn. J. Pharmacol.; 89: 193-196; cited in a prior Office Action); and WHO ("Definition, Diagnosis and Classification of Diabetes mellitus and its Complications"; 1999; World Health Organization; Department of Noncommunicable Disease Surveillance. Geneva; pp. 1-59; accessed online on 12/9/2009 at: http://whqlibdoc.who.int/hq/1999/WHO_NCD_NCS_99.2.pdf); in view of Ortlepp et al. ("Inhibition of the rennin-angiotensin system ameliorates genetically determined hyperinsulinemia"; 2002; European Journal of Pharmacology; 436: 145-150: IDS 3/25/2008 reference 1; cited in a prior Office Action).

Imura teaches the administration a fibrogen lowering agent, which is a compound having angiotensin II antagonist activity, useful as a therapeutic agent for various diseases (abstract); compounds taught include candesartan cilexetil, administered to rats at concentrations of 1 mg/kg (correspond dose of about 70 mg for a human adult; paragraphs 0210, 0213; claims 6, 18); formulations for administration contain candesartan cilexetil at 30 mg (Tables 1 and 2); the agents of the invention are useful as prophylactic or therapeutic agents for fibrinogen-related diseases of mammals, which includes metabolic disorders, such as Syndrome X (paragraph 0156); mammals specifically include men (paragraph 0104) and humans (paragraphs 0156, 0165); compounds with angiotensin II antagonistic activity include formula I', with selection (3) of paragraph 0095 has a very similar core structure as instant compound I:4 (paragraphs 0094-96); preferred dosages of this formula are 0.1-50 mg, once to three times a day (paragraph 0155). Imura does not teach the compound currently under

examination, compound I:4, or the metabolic syndrome criteria required by the last four lines of instant claim 11.

As is present on the record, Yoneyama teaches L-158,809 is a new angiotensin II type 1 receptor antagonist (abstract) (the record indicates that L 158809 is a common name used for compound I:4); blood pressure reduction is shown for 0.03 mg/kg, 0.3 mg/kg and 3 mg/kg (p. 194, Figure 1). 0.03 mg/kg administered to a 70 kg human would correspond to 2.1 mg dosage; 3 mg/kg administered to a 70 kg human would correspond to a 210 mg dosage. This reference established that compound I:4 has activity in reducing blood pressure in humans, and the compound's mechanism is as an angiotensin II type 1 receptor antagonist.

WHO teaches diagnostic criteria for diabetes mellitus (title) and metabolic syndrome (p. 31, subtitle); the working definition includes glucose intolerance, IGT or diabetes mellitus and/or insulin resistance together with two or more components listed (p. 32, section 8.1, 1st paragraph); impaired glucose regulation or diabetes is given by Table 1; named criteria include: insulin resistance includes glucose uptake below lowest quartile; raised arterial pressure ≥140/90 mmHg; raised plasma triglycerides (≥ 1.7 mmol l^{-1}) and/or low HDL-cholesterol (<0.9 mmol l^{-1} in men; <1.0 mmol l^{-1} in women); BMI >30 kg/m^2, (p. 32-33, section 8.1); with respect to the impaired glucose regulation component, the diagnostic criteria for diabetes mellitus include a fasting plasma glucose concentration in whole blood of 6.1 mmol l^{-1} and above (p. 5, section 2.3.1, 1st paragraph). This teaching establishes that the diagnostic criteria parameters recited in the last four lines of claim 11 are recognized diagnostic criteria for metabolic syndrome;

i.e., it would have been obvious to select a human patient with elevated insulin levels and high blood pressure at levels taught and at least one more of the required parameters, an individual that would have been diagnosed with metabolic syndrome according to WHO criteria, to whom the instant method of treating metabolic syndrome would have been applied.

The record also indicates that Ortlepp teaches the effects of the angiotensin II receptor antagonist irbesartan on the metabolic syndrome in an animal model, concluding long term treatment with an angiotensin-converting enzyme inhibitor or an angiotensin II receptor antagonist can ameliorate obesity and hyperinsulinemia in a genetically determined mouse model (abstract).

It would have been obvious to one of ordinary skill in the art at the time of the invention to administer compound I:4 in place of irbesartan in the treatment of metabolic syndrome taught by Ortlepp or in place of the angiotensin II antagonist compounds candesartan cilexetil or formula I compounds of Imura, to a patient with the required WHO diagnostic parameters for metabolic syndrome, i.e., a human patient with elevated insulin levels and high blood pressure at levels recited, and at least one more of the required parameters, giving the method of instant claim 11. It would also have been obvious to optimize the amount dosed based on a reduction of the elevated insulin levels and other metabolic syndrome parameters characteristic of the individual being treated, this optimization would have been expected to give dosages within the ranges of instant claims 17-20, especially since dosages within this range are already taught or rendered obvious for compounds related to compound I:4, as discussed above. The

motivation to substitute Compound I:4 for irbesartan, candesartan cilexetil or a formula I compound would have been the substitution of one art-recognized equivalent compound (Compound I:4) for another (irbesartan, candesartan cilexetil or a formula I compound) in terms of the angiotensin II receptor antagonist activity. The motivation to optimize the dosages would have been the routine optimization of amounts used for reduction of insulin levels, blood pressure and other metabolic syndrome symptoms.

Conclusion

6. No claim is allowed.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to TIMOTHY P. THOMAS whose telephone number is (571)272-8994. The examiner can normally be reached on Monday-Thursday 6:30 a.m. - 5:00 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brandon Fetterolf can be reached on (571) 272-2919. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Timothy P Thomas/
Examiner, Art Unit 1628